

## REMARKS

### I. Amendments to Claims

Support for the amendments is found throughout the specification and claims as originally filed. No new matter is believed to have been introduced, and entry of these amendments is respectfully requested. Applicants believe that the amended claims define the invention in a manner supported by the original application, and in a manner so as to render moot certain of the Office Action rejections as set out in greater detail below.

Claim 1, drawn to a method of treating acne conditions, combines original claim 1 and original claim 2. The claim now recites that the antimicrobial metal in contact with the problem area of the patient is characterized by sufficient atomic disorder such that the metal, in contact with an alcohol or water based electrolyte, releases atoms, ions, molecules, or clusters of the antimicrobial metal at a concentration sufficient to provide a localized antimicrobial and anti-inflammatory effect.

Original claim 2 has been cancelled.

Claim 3 incorporates the definition of “nanocrystalline” to indicate a grain size which is less than 100 nanometers in at least one dimension. The dependency has also been amended. Support is found in the specification on page 9, lines 15 - 19.

New claim 13, dependent upon claim 3, incorporates the definition of “nanocrystalline” to indicate a grain size which is less than 50 nanometers in at least one dimension. Support is found in the specification on page 9, lines 15 - 19.

New claim 14, dependent upon claim 13, incorporates the definition of “nanocrystalline” to indicate a grain size which is less than 25 nanometers in at least one dimension. Support is found in the specification on page 9, lines 15 - 19.

The dependency of claim 4 has been amended to claim 3.

New claim 15, dependent upon claim 5, indicates a particulate size which is less than 100  $\mu\text{m}$ . Support is found in the specification on page 9, lines 20 - 23.

New claim 16, dependent upon claim 15, indicates a particulate size which is less than 40  $\mu\text{m}$ . Support is found in the specification on page 9, lines 20 - 23.

## **II. Rejections under 35 USC §112**

The Office Action alleges that original claims 3, 5, 6, 9, 10, 11 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Office Action alleges that the term “nanocrystalline” is indefinite because the specification indicates size parameters but states exclusion of such size parameters when used as a powder. Applicants respectfully disagree with the objection, but have amended the claims for further clarity.

For clarity, Applicants have amended original claim 3 to incorporate the definition of “nanocrystalline” as originally presented in the specification on page 9, lines 15 - 19. Applicants emphasize that the term “nanocrystalline” is defined as single-phase or multi-phase polycrystals having a specific grain size. The grain size is less than 100 nanometers, more preferably less than 50 nanometers and most preferably less than 25 nanometers in at least one dimension. The term, as applied to the grain size in the crystal lattice of coatings, powders or flakes of the antimicrobial metals, is not meant to restrict the particle size of the materials when used in a powder form. Thus, in the phrase “nanocrystalline powder,” the term “nanocrystalline” refers to the grain size in the crystal lattice, not the particulate size of the powder. New claim 13 thus indicates a grain size which is preferably less than 50 nanometers in at least one dimension, while new claim 14 indicates a grain size which is more preferably less than 25 nanometers in at least one dimension.

Applicants believe that amendment of original claim 3 obviates the rejection of original claim 5. Applicants have also added new claims 15 and 16 to define the preferred particulate sizes. Powders of the antimicrobial metals are preferably sized at less than 100  $\mu\text{m}$ , and more preferably less than 40  $\mu\text{m}$ . New claim 15 indicates a particulate size which is preferably less than 100  $\mu\text{m}$ . New claim 16 indicates a particulate size which is preferably less than 40  $\mu\text{m}$ . Support is found in the specification on page 9, lines 20 - 23.

Applicants respectfully submit that the claim amendments which clarify the definition of wording such as “nanocrystalline” have not altered the scope of these claims, since these items were originally defined in the application as filed. In view of the amendment to original claim 3,

withdrawal of the rejection of all claims dependent thereon, including original claims 5, 6, 9, 10, 11 and 12 is thus respectfully requested.

### **III. Rejections under 35 USC §103**

The Office Action alleges that original claims 1 - 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over International Publication No. WO 95/13704 (Burrell, R.E., Apte, P.S., Gill, K.S., Precht, R.J., Morris, L.R., McIntosh, C.L. and Sant, S.B. Anti-microbial materials. Published May 26, 1995) in view of Chinese Patent No. 1262093 (Shu. Silver foil cosmetics. Published August 9, 2000). The Office Action alleges that International Publication No. WO 95/13704 discloses a fine grain antimicrobial material, having a grain size less than 200 nm, characterized by sufficient atomic disorder such that a sustained release of material, i.e. metals such as silver, gold, platinum and palladium, provide a localized antimicrobial effect when in contact with an alcohol or water electrolyte. The Office Action particularly points out claims 47, 49 and the subsequent claims of International Publication No. WO 95/13704. Further, the Office Action alleges that Chinese Patent No. 1262093 establishes that silver disinfectant particles are known to be used to treat acne. The Office Action thus alleges that the claimed invention, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made, since the Office Action alleges that every element of the invention has been fairly suggested by the combined teachings of the cited references.

Applicants respectfully traverse this rejection based on International Publication No. WO 95/13704 and the abstract of Chinese Patent No. 1262093 in view of the clarifying amendments to the claims, and the reasons set out below.

As indicated above, Applicants have combined original claims 1 and 2 such that amended claim 1 now recites that the antimicrobial metals are characterized by atomic disorder. As defined in the specification on page 7, lines 20 - 24, the term "atomic disorder" is defined as including high concentrations of: point defects in a crystal lattice, vacancies, line defects such as dislocations, interstitial atoms, amorphous regions, grain and sub grain boundaries and the like relative to its normal ordered crystalline state. Atomic disorder leads to irregularities in surface topography and inhomogeneities in the structure on a nanometer scale. This feature enables the

metal, in contact with an alcohol or water based electrolyte, to release atoms, ions, molecules, or clusters of the antimicrobial metal at a concentration sufficient to provide, surprisingly, a combined antimicrobial and anti-inflammatory effect.

Applicants have only the abstract of Chinese Patent No. 1262093. According to the abstract, Chinese Patent No. 1262093 relates to a kind of silver foil cosmetic prepared by adding silver foil to dispersing medium, stirring to generate fine silver foil particles of 0.1 - 4.5 microns in thickness and 0.00001 - 0.1 sq cm in area, and adding the particles to different cosmetics. The abstract also alleges that the silver foil cosmetic has inflammation-relieving and disinfecting action for curing acne, and can make skin weakly acidic for improving skin metabolism. However, Applicants see no mention in the abstract of Chinese Patent No. 1262093 of antimicrobial metals characterized by atomic disorder, as recited in claim 1 of Applicants' application.

International Publication No. WO 95/13704 relates to antimicrobial coatings, foils and powders and methods for their production. Antimicrobial metals are used to confer an antimicrobial effect. No other utility is set forth for the materials of the cited reference. In contrast, claim 1 of the Applicants' instant application recites a method of treatment of acne conditions by contacting the problem area with antimicrobial metals which provide a localized antimicrobial and anti-inflammatory effect. Applicants see no mention in International Publication No. WO 95/13704 of anti-inflammatory effects, treatment of acne conditions using antimicrobial metals, or antimicrobial metals which provide combined antimicrobial and anti-inflammatory effects.

While the cited CN abstract indicates that the use of silver foil particles has an antimicrobial and inflammatory relieving effect, the cited PCT application by Burrell *et al.*, provides conclusive evidence to the contrary, which cannot be ignored. Example 2 of WO 95/13704 includes conclusive comparative data showing that silver materials such as rolled silver sheet, silver wire, silver membrane cast, sputtered silver films formed under conditions not sufficient to produce atomic disorder, do not provide a useful antimicrobial effect (all of these material provided a zone of inhibition (ZOI) less than 0.5 mm). Furthermore, Example 10 of WO 95/13704 demonstrates with conclusive comparative data that nanocrystalline sized powders

of silver (actually finer size than the cited CN reference) did not provide a useful, sustainable antimicrobial effect. It was only when such powders were cold worked to introduce atomic disorder that a useful antimicrobial effect, that was also sustainable over time, was achieved. Finally, Example 25 of WO 95/13704 demonstrates that bulk silver (i.e., silver in its normal ordered crystalline state) did not provide a useful antimicrobial effect, producing ZOI data of less than 1 mm. WO 95/13704 makes it clear that a ZOI of less than about 1 mm is not a useful antimicrobial effect (see page 11, lines 12-19).

Thus, Applicants respectfully submit that a combination of the teachings of the two cited references would lead one skilled in the art to conclude that fine silver foil particles alone, without atomic disorder, would not possess useful properties for any antimicrobial-based problem. This is in accord with the history of the use of silver to treat infection. Silver metal alone does not provide a useful result. The history of the use of silver to treat infection is detailed in the background section of WO 95/13704. Something more was needed - ex. use of soluble silver salts such as silver nitrate, galvanic action with a more noble metal, use of electrical activation etc.

It was only in the present application that Applicants went on to prove that not only did atomically disordered silver provide a useful antimicrobial effect in the specific case of acne, but that it also provided a surprising anti-inflammatory effect against acne. This combination of activities for materials of the present invention is not found in the prior art.

In summary, none of the cited references is believed to anticipate any of the claims of the present application. No combination of any of the cited prior art is warranted, since none of the references show the features of the invention as claimed (i.e., antimicrobial metals with atomic disorder and having both antimicrobial and anti-inflammatory effects for the treatment of acne conditions) in the present application.

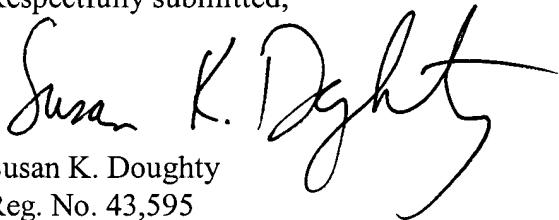
The amended claims are believed to be definite and are believed to overcome the rejections in the Office Action. Accordingly, reconsideration and allowance of the subject application are respectfully requested.

Conclusion

This response is accompanied by a Petition for Extension of Time of one month and a check in the amount of \$110.00 for the requisite fee.

It is believed that no other fees, including claim fees, are required. If the enclosed amount submitted is incorrect, please deduct any deficiency, including the fee for any additional extensions of time required, or credit any overpayment to deposit account no. 07-1969.

Respectfully submitted,

  
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1. (Once amended) A method of treating acne conditions, which comprises:  
contacting an acne problem area of a patient, with a therapeutically effective amount of one or more antimicrobial metals in a crystalline form to provide a localized antimicrobial and anti-inflammatory effect, wherein the one or more antimicrobial metals are characterized by sufficient atomic disorder, such that the metal, in contact with an alcohol or water-based electrolyte, releases atoms, ions, molecules, or clusters of at least one antimicrobial metal at a concentration sufficient to provide a localized antimicrobial and anti-inflammatory effect.
2. [Cancelled]
3. (Once amended) The method as set forth in claim [2] 1, wherein the antimicrobial metal is nanocrystalline silver, wherein nanocrystalline indicates a grain size which is less than 100 nanometers in at least one dimension.
4. (Once amended) The method as set forth in claim [1]3, wherein the one or more antimicrobial metals are provided as a coating on, or filler in, a dressing, or in a pharmaceutical composition with one or more pharmaceutically and dermatologically acceptable carriers, diluents, or excipients suitable for topical application.